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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,383	06/13/2007	Cathy Lofton-Day	47675-065US0	3836

22504 7590 11/26/2010

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EXAMINER	
LU, FRANK WEI MIN	

ART UNIT	PAPER NUMBER
1634	

NOTIFICATION DATE	DELIVERY MODE
11/26/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/562,383	LOFTON-DAY ET AL.	
	Examiner	Art Unit	
	FRANK W. LU	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 September 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10-43,45-51,53,55 and 57-59* is/are pending in the application.

4a) Of the above claim(s) *5,6,27,32,38,43,46-51,53,55 and 57-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7,8,10-26,28-31,33-37,39-42 and 45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 December 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/18/2006, 4/7/2008, and 10/4/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of species (1) (said expression level is determined by detecting the presence, absence or level of mRNA transcribed from said gene or sequence, see claim 4) in the reply filed on September 13, 2010 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Since applicant has elected Group I, SEQ ID NOs: 5, 312, 313, 428, and 429 in the response filed on January 7, 2010 and claims 9 and 44 have been canceled, claims 1-4, 7, 8, 10-26, 28-31, 33-37, 39-42, and 45 will be examined.

Priority

2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in European Patent Office on February 27, 2004 (04090072.2) and an application filed in United Kingdom Patent Office on May 6, 2004 (04090175.3). It is noted, however, that applicant has not filed certified copies of these application as required by 35 U.S.C. 119(b).

Specification

3. The disclosure is objected to because of the following informality: since cases 10/679,062, 10/603,138, and 10/602,494 have been abandoned, applicant is required to update these information in the first paragraph of the specification

Appropriate correction is required.

Claim Objections

4. Claim 2 or 3 or 8 is objected to because of the following informality: "the ALX 4 gene sequence" should be "ALX 4 gene sequence".

5. Claim 4 is objected to because of the following informality: "sequence" in line 2 should be "gene sequence thereof".

6. Claim 7 is objected to because of the following informality: "sequence" in line 3 should be "gene sequence thereof".

7. Claim 12 or 13 or 14 or 15 or 17 or 18 or 20 is objected to because of the following informality: "SEQ ID NOS:5" should be "SEQ ID NO:5".

8. Claim 12 or 13 or 14 or 15 or 16 or 17 or 18 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim because SEQ ID NO: 5 is 100% identical to human ALX 4 gene sequence. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

9. Claim 21 is objected to because of the following informality: SEQ ID NOs: 304-535 and 65-88 should be deleted since they have not been selected by applicant.

10. Claim 23 is objected to because of the following informalities: (1) "contacting or amplifying in c)" should be "the amplification in c)"; and (2) "a amplificate nucleic acid molecule carrying a detectable label" should be "an amplificate nucleic acid molecule carrying a detectable label"

11. Claim 24 is objected to because of the following informality: "the detectable amplificate label" should be "the detectable label".

12. Claim 21 or 26 or 28 or 29 or 31 or 40 or 42 is objected to because of the following informality: the phrase "in each case" should be deleted.

13. Claim 33 is objected to because of the following informality: "at least one such hybridizing nucleic acid molecule or peptide nucleic acid molecule" should be "the at least one hybridizing nucleic acid molecule or peptide nucleic acid molecule".

14. Claim 35 is objected to because of the following informality: "at least one such hybridized nucleic acid molecule" should be "the at least one hybridized nucleic acid molecule".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Enablement

Claims 1-4, 7, 8, 10-26, 28-31, 33-37, 39-42, and 45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The claims are drawn to a method for detecting and/or for detecting and distinguishing among colon cell proliferative disorders in a subject and a method for detecting and/or for detecting and distinguishing between or among colon cell proliferative disorders and healthy tissues in a subject. The invention is a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." *Mycogen Plant Sci., Inc. v. Monsanto Co.,* 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The Breadth of The Claims

Claims 1, 2, and 18 encompass a method for detecting and/or for detecting and distinguishing among colon cell proliferative disorders in any kind of subject by contacting genomic DNA isolated from blood plasma, blood serum, whole blood, isolated blood cells, or cells isolated from the blood obtained from the subject with at least one reagent, or series of reagents that distinguishes between methylated and non-methylated CpG dinucleotides within at least one target region of the genomic DNA. Claim 2 further limits claim 1 and requires that the target region comprises, or hybridizes under stringent conditions to at least 16 contiguous nucleotides of the ALX 4 gene sequence. Claims 3, 4, and 7 encompass a method for detecting and/or for detecting and distinguishing among colon cell proliferative disorders in any kind of subject by determining, in a biological sample isolated from the subject, the expression levels of the ALX 4 gene or gene sequences thereof. Claim 4 further limits claim 3 and requires that said

expression level is determined by detecting the presence, absence or level of mRNA transcribed from said gene or sequence. Claim 7 further limits claim 3 and requires that said expression is determined by detecting the presence or absence of CpG methylation within said gene or sequence. Claims 8, 10-17, 19, 21-26, 28-31, 33-37, and 39-42 encompass a method for detecting and/or for detecting and distinguishing among colon cell proliferative disorders in any kind of subject by contacting genomic DNA isolated from a biological sample obtained from the subject with at least one reagent, or series of reagents that distinguishes between methylated and non-methylated CpG dinucleotides within at least one target region of the genomic DNA, wherein the at least one target region comprises, or hybridizes under stringent conditions to a sequence of at least 16 contiguous nucleotides of the ALX 4 gene sequence. Claim 20 encompasses a method for detecting and/or for detecting and distinguishing between or among colon cell proliferative disorders and healthy tissues in a subject comprising contacting genomic DNA isolated from a biological sample obtained from the subject with at least one reagent, or series of reagents that distinguishes between methylated and non-methylated CpG dinucleotides within at least one target region of the genomic DNA, wherein the at least one target region comprises, or hybridizes under stringent conditions to a sequence of at least 16 contiguous nucleotides of at least two sequences selected from the group consisting of SEQ ID NO:5 and complements thereof. Claim 45 encompasses a method for detecting and/or for detecting and distinguishing among colon cell proliferative disorders in any kind of subject by determining, based on a presence or absence of, or on property of at least one of said cleavage fragments, the methylation state of at least one CpG dinucleotide of a sequence consisting of SEQ ID NO:5, or

an average, or a value reflecting an average methylation state of a plurality of CpG dinucleotides of a sequence consisting of SEQ ID NO:5.

Working Examples

The specification provides no working example related to the claimed invention recited in claims 1-3, 7, 8, 10-26, 28-31, 33-37, 39-42, and 45.

The Amount of Direction or Guidance Provided and The State of The Prior Art

The specification does not provide guidance for the methods recited in claims 1-3, 7, 8, 10-26, 28-31, 33-37, 39-42, and 45. Furthermore, there is no experimental condition and/or experimental data in the specification to support the claimed invention recited in claims 1-3, 7, 8, 10-26, 28-31, 33-37, 39-42, and 45. Although it is known in the art that that "age-related methylation is a common event in human tissue" (see page 351, left column, second paragraph from Seminars in Cancer Biology, 9, 349-357, 1999) and "[M]ethylation changes in cancer include hypomethylation of overall genomic DNA as well as regional hypermethylation involving CpG islands" (see page 349, right column, second paragraph from Seminars in Cancer Biology, 9, 349-357, 1999), and ALX 4 gene methylation is a potential marker for colorectal adenocarcinomas (Gastroenterology, 131, 1418-1430, 2006), during the process of the prior art search, the examiner has not found any prior art which is related to the claimed invention recited in claims 1-3, 7, 8, 10-26, 28-31, 33-37, 39-42, and 45.

Level of Skill in The Art, The Unpredictability of The Art, and The Quantity of Experimentation Necessary

While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability whether the methods recited in claims 1-3, 7, 8, 10-26, 28-31, 33-37, 39-42, and 45 can be performed.

First, since it is known that "age-related methylation is a common event in human tissue" (see page 351, left column, second paragraph from Seminars in Cancer Biology, 9, 349-357, 1999) and "[M]ethylation changes in cancer include hypomethylation of overall genomic DNA as well as regional hypermethylation involving CpG islands" (see page 349, right column, second paragraph from Seminars in Cancer Biology, 9, 349-357, 1999) and claim 1 does not limit the target region of the genomic DNA to a specific region of a specific gene, it is unclear how the presence of methylated CpG dinucleotides within at least one of any target region of the genomic DNA isolated from blood plasma, blood serum, whole blood, isolated blood cells, or cells isolated from the blood obtained from a subject must indicate the presence of a colon cell proliferative disorder such as colon cancer in the subject and cannot indicate that the subject such as a human is a subject with old age. For example, it is known that CpG methylation of estrogen receptor gene has been found in both normal aged colon mucosa and colon cancer (see page 350, right column from Seminars in Cancer Biology, 9, 349-357, 1999). Furthermore, since claim 1 does not indicate what kind of differences exist in methylated CpG dinucleotides within at least one target region of the genomic DNA isolated from blood plasma, blood serum, whole blood, isolated blood cells, or cells isolated from the blood among different cell proliferative disorders, it is unclear how to detect and/or detect and distinguish among colon cell proliferative disorders

in the subject as recited in claims 1, 2, and 18. In addition, since methylated CpG dinucleotides only exist in mammals (see "DNA methylation" from Wikipedia, the free encyclopedia) and it is unclear whether all mammals have colon cell proliferative disorders, it is unclear how to detect and/or detect and distinguish among colon cell proliferative disorders in any kind of subject as recited in claims 1, 2, and 18.

Second, since claims 3, 4, and 7 do not indicate what kind of differences exist in the expression levels of the ALX 4 gene or gene sequences thereof among colon cell proliferative disorders in a subject and the specification does not show what kind of differences exist in the mRNA expression levels of the ALX 4 gene or gene sequences thereof among colon cell proliferative disorders in a subject, it is unclear how to detect and/or detect and distinguish among colon cell proliferative disorders in the subject as recited in claims 3, 4, and 7. Furthermore, since methylated CpG dinucleotides only exist in mammals (see "DNA methylation" from Wikipedia, the free encyclopedia) and it is unclear whether all mammals have colon cell proliferative disorders, it is unclear how to detect and/or detect and distinguish among colon cell proliferative disorders in any kind of subject as recited in claims 3, 4, and 7.

Third, since claims 8, 10-17, 19-26, 28-31, 33-37, and 39-42 do not indicate what kind of differences exist in methylated CpG dinucleotides within at least one target region of the genomic DNA isolated from a biological sample among different cell proliferative disorders wherein the at least one target region comprises, or hybridizes under stringent conditions to a sequence of at least 16 contiguous nucleotides of ALX 4 gene sequence, it is unclear how to detect and/or detect and distinguish among colon cell proliferative disorders in the subject as recited in claims 8, 10-17, 19-26, 28-31, 33-37, and 39-42. Furthermore, since methylated CpG

dinucleotides only exist in mammals (see "DNA methylation" from Wikipedia, the free encyclopedia) and it is unclear whether all mammals have colon cell proliferative disorders, it is unclear how to detect and/or detect and distinguish among colon cell proliferative disorders in any kind of subject as recited in claims 8, 10-17, 19-26, 28-31, 33-37, and 39-42.

Fourth, since claim 21 requires contacting the treated genomic DNA, or the treated fragment thereof, with an amplification enzyme and at least two primers comprising, a contiguous sequence of at least 9 nucleotides that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NOS:312, 313, 428 and 429, if the two primers are "TTTTTTTTTT" from SEQ ID NOS: 313 and 429 which can hybridize polyA sequence of many different mRNAs, step c) of claim 21 cannot form a specific amplification product of human ALX 4 gene so that step d) of claim 21 cannot be performed. Furthermore, from claim 21, it is unclear how at least one of detecting, or detecting and distinguishing between colon cell proliferative disorders can be, at least in part, afforded by determining, based on a presence or absence of, or on a property of said amplificate, the methylation state of at least one CpG dinucleotide of a sequence consisting of SEQ ID NOS:5 or how at least one of detecting, or detecting and distinguishing between colon cell proliferative disorders can be, at least in part, afforded by determining, based on an average, or a value reflecting an average methylation state of a plurality of CpG dinucleotides of a sequence consisting of SEQ ID NOS:5.

Fifth, since claims 39-42 requires hybridizing at least one nucleic acid molecule comprising a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under stringent conditions to a sequence selected from the group consisting of SEQ

ID NOS:312, 313, 428 and 429, if the nucleic acid molecule is "TTTTTTTTT" from SEQ ID NO: 313 or 429 which can hybridize polyA sequence of many different mRNAs, claims 39-42 cannot form a specific hybridization complex for human ALX 4 gene so that the methods of claims 49-42 cannot be performed.

Sixth, since claim 20 does not indicate what kind of differences exist in methylated CpG dinucleotides within at least one target region of the genomic DNA isolated from a biological sample between or among colon cell proliferative disorders and healthy tissues wherein the at least one target region comprises, or hybridizes under stringent conditions to a sequence of at least 16 contiguous nucleotides of at least two sequences selected from the group consisting of SEQ ID NO:5 and complements thereof, it is unclear how to detect and/or detect and distinguish between or among colon cell proliferative disorders and healthy tissues in the subject as recited in claim 20. Furthermore, since methylated CpG dinucleotides only exist in mammals (see "DNA methylation" from Wikipedia, the free encyclopedia) and it is unclear whether all mammals have colon cell proliferative disorders, it is unclear how to detect and/or detect and distinguish between or among colon cell proliferative disorders and healthy tissues in any kind of subject as recited in claim 20.

Seventh, since claim 45 does not indicate what kind of differences exist in cleavage fragments among colon cell proliferative disorders, it is unclear how at least one of detecting, or of detecting and differentiating among colon cell proliferative disorders can be afforded by determining, based on a presence or absence of, or on property of at least one such cleavage fragment, the methylation state of at least one CpG dinucleotide of a sequence consisting of SEQ ID NO:5 or how at least one of detecting, or of detecting and differentiating

among colon cell proliferative disorders can be afforded by determining, based on an average, or a value reflecting an average methylation state of a plurality of CpG dinucleotides of a sequence consisting of SEQ ID NO:5 as recited in claim 45. Furthermore, since methylated CpG dinucleotides only exist in mammals (see "DNA methylation" from Wikipedia, the free encyclopedia) and it is unclear whether all mammals have colon cell proliferative disorders, it is unclear how to detect and/or detect and distinguish among colon cell proliferative disorders in any kind of subject as recited in claim 45.

For the reasons discussed above, it would have required undue experimentation for one skilled in the art at the time of the invention to practice over the full scope of the invention claimed. The undue experimentation at least includes to test whether the methods recited in claims 1-4, 7, 8, 10-26, 28-31, 33-37, 39-42, and 45 can be performed.

Conclusion

In the instant case, as discussed above, the level of unpredictability in the art is high, the specification provides one with no guidance that leads one to claimed methods. One of skill in the art cannot readily anticipate the effect of a change within the subject matter to which the claimed invention pertains. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of any working example related to the claimed invention and the no teaching in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

17. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

18. Claims 1-4, 7, 8, 10-26, 28-31, 33-37, 39-42, and 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

19. Claim 1 is rejected as vague and indefinite because the phrase "detecting and distinguishing between or among colon cell proliferative disorders" in the preamble and step b) does not sense because the word "between" is used to compare two objects and is not used to compare more than two objects. Does this phrase mean "detecting and distinguishing among colon cell proliferative disorders"? Please clarify.

20. Claim 1 or 8 or 20 recites the limitation "said contiguous nucleotides" in the claim. There is insufficient antecedent basis for this limitation in the claim because there is no phrase "contiguous nucleotides" before "said contiguous nucleotides". Please clarify.

21. Claim 4 is rejected as vague and indefinite because the phrase "detecting and distinguishing between or among colon cell proliferative disorders" in the preamble does not sense because the word "between" is used to compare two objects and is not used to compare more than two objects. Does this phrase mean "detecting and distinguishing among colon cell proliferative disorders"? Please clarify.

22. Claim 7 is rejected as vague and indefinite because it is unclear hypermethylation in where indicates the presence of a colon cell proliferative disorder. Please clarify.

23. Claim 8 is rejected as vague and indefinite because the phrase "detecting and distinguishing between or among colon cell proliferative disorders" in the preamble and lines 8

and 9 does not sense because the word "between" is used to compare two objects and is not used to compare more than two objects. Does this phrase mean "detecting and distinguishing among colon cell proliferative disorders"? Please clarify.

24. Claim 10 or 11 is rejected as vague and indefinite because colon adenoma, normal colon tissue, non-colon tissues and non-colon cell proliferative disorders are not conditions. Please clarify.

25. Claim 10 is rejected as vague and indefinite. Since "wherein" phrase is used to define the phrase or word that appears before and there is no colorectal carcinoma in claim 8, it is unclear why colorectal carcinoma can be distinguished from the group consisting of colon adenoma, normal colon tissue, non-colon tissues and non-colon cell proliferative disorders. Please clarify.

26. Claim 11 is rejected as vague and indefinite. Since "wherein" phrase is used to define the phrase or word that appears before and there is no colon carcinoma in claim 8, it is unclear why colon adenoma can be distinguished from the group consisting of colon carcinoma, normal colon tissue, non-colon tissues and non-colon cell proliferative disorders. Please clarify.

27. Claim 12 is rejected as vague and indefinite. Since "wherein" phrase is used to define the phrase or word that appears before and there is no colorectal carcinoma tissue or colon adenomas in claim 8, it is unclear why carcinoma tissue or colon adenomas can be distinguished from at least one tissue selected from the group consisting of colon polyps less than lcm in diameter, inflammatory colon tissue, and normal colon tissue. Please clarify.

28. Claim 13 is rejected as vague and indefinite. Since "wherein" phrase is used to define the phrase or word that appears before and there is no colorectal carcinoma in claim 8, it is unclear why colorectal carcinoma can be distinguished from at least one tissue selected from the group

consisting of non-colon healthy tissue, peripheral blood lymphocytes and non-colon cancer tissue. Please clarify.

29. Claim 14 is rejected as vague and indefinite. Since "wherein" phrase is used to define the phrase or word that appears before and there is no colorectal carcinoma in claim 8, it is unclear why colorectal carcinoma can be distinguished from at least one tissue selected from the group consisting of inflammatory colon tissue, normal colon tissue, non-colon healthy tissue, peripheral blood lymphocytes, colon adenomas and non-colon cancer tissue. Please clarify.

30. Claim 15 is rejected as vague and indefinite. Since "wherein" phrase is used to define the phrase or word that appears before and there is no colorectal carcinoma in claim 8, it is unclear why colorectal carcinoma can be distinguished from colon adenoma. Please clarify.

31. Claim 16 is rejected as vague and indefinite. Since "wherein" phrase is used to define the phrase or word that appears before and there is no colorectal carcinoma tissue or large adenomas in claim 8, it is unclear why at least one of colorectal carcinoma tissue, or large adenomas can be distinguished from at least one tissue selected from the group consisting of inflammatory colon tissue, and normal colon tissue. Please clarify.

32. Claim 17 is rejected as vague and indefinite. Since "wherein" phrase is used to define the phrase or word that appears before and there is no colorectal carcinoma tissue in claim 8, it is unclear why colorectal carcinoma tissue can be distinguished from at least one of inflammatory colon tissue and normal colon tissue. Please clarify.

33. Claim 18 is rejected as vague and indefinite. Since "wherein" phrase is used to define the phrase or word that appears before and there is no colorectal carcinoma tissue, or colon adenomas in claim 8, it is unclear why least one of colorectal carcinoma tissue, or colon

adenomas can be distinguished from at least one tissue selected from the group consisting of inflammatory colon tissue, normal colon tissue, non-colon healthy tissue, peripheral blood lymphocytes, and non-colon cancer tissue. Please clarify.

34. Claim 18 is rejected as vague and indefinite. Since "wherein" phrase is used to define the phrase or word that appears before and there is no tissues originating from the colon in claim 8, it is unclear why tissues originating from the colon can be distinguished from tissues of non-colon origin. Please clarify.

35. Claim 19 recites the limitation "the colon" in the claim. There is insufficient antecedent basis for this limitation in the claim because there is no word "the colon" in claim 8. Please clarify.

36. Claim 21 is rejected as vague and indefinite because it is unclear how to correlate with the step of contacting genomic DNA isolated from a biological sample obtained from a subject with at least one reagent, or series of reagents that distinguishes between methylated and non-methylated CpG dinucleotides within at least one target region of the genomic DNA in claim 20 with steps a) to d) of claim 21. Please clarify.

37. Claim 21 is rejected as vague and indefinite in view of step d) because SEQ ID No: 5 is not a group or groups. Please clarify.

38. Claim 23 is rejected as vague and indefinite because it is unclear what is the relationship between at least one amplificate in claim 21 and an amplificate nucleic acid molecule carrying a detectable label in claim 23. Please clarify.

39. Claim 34 is rejected as vague and indefinite. Since claim 31 only has one hybridizing nucleic acid molecule or peptide nucleic acid molecule, it is unclear why claim 34 has a plurality

of such hybridizing nucleic acid molecules or peptide nucleic acid molecules and claims 31 and 34 do not correspond each other. Please clarify.

40. Claim 34 is rejected as vague and indefinite because the phrase "a nucleic acid or peptide nucleic acid array selected from the array group consisting of linear or substantially so, hexagonal or substantially so, rectangular or substantially so, and combinations thereof" does not make sense. Does this phrase mean a nucleic acid or peptide nucleic acid array selected from the array group consisting of linear array, hexagonal array and rectangular array? Please clarify.

41. Claim 37 is rejected as vague and indefinite because it is unclear what is the relationship between at least two primers in claim 21 and methylation-specific primers in claim 37. Please clarify.

42. Claim 39 or 41 is rejected as vague and indefinite because it is unclear what is the relationship between at least two primers in claim 21 and primer oligonucleotides comprising one or more CpG; TpG or CpA dinucleotides in claim 39 or 41. Please clarify.

43. Claim 39 or 40 or 42 is rejected as vague and indefinite because it is unclear that the at least one nucleic acid molecule or peptide nucleic acid molecule hybridizes to what. Please clarify.

44. Claim 41 is rejected as vague and indefinite because it is unclear that the at least one detectably labeled nucleic acid molecule hybridizes to what. Please clarify.

45. Claim 45 is rejected as vague and indefinite because the phrase "detecting and distinguishing between or among colon cell proliferative disorders" in the preamble and step d) does not sense because the word "between" is used to compare two objects and is not used to

compare more than two objects. Does this phrase mean "detecting and distinguishing among colon cell proliferative disorders"? Please clarify.

Conclusion

46. No claim is allowed.

47. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen, can be reached on (571)272-0731.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Frank W Lu /
Primary Examiner, Art Unit 1634
November 22, 2010